Donor's genotype controls the differentiation of iPS cells—source tissue insignificant

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Pluripotent stem cells derived from different cell types are equally susceptible to reprogramming, indicates a recent study.

Published in the *Stem Cell Reports* journal, the results of the study disprove the assumption that an "epigenetic memory" of cells from different tissue types would significantly impact the differentiation of induced pluripotent stem (iPS) cells.

Under laboratory conditions, iPS cells can be derived from human cells. Such iPS cells can be cultivated in unlimited amounts, and if necessary, they can be made to differentiate into desired cell types, such as heart, liver or nerve cells.

Medical research can use induced pluripotent cells in many different ways - for example, to study the mechanisms of disease or in drug screenings - which makes them perfect biobanking material. Such iPS cells can be derived, e.g., from fibroblasts cultivated from a piece of skin, or directly from blood cells. Blood cells are the most useful biobank material, as taking blood samples is a simple process, routinely done in the course of diagnostics and treatment.

However, it has thus far been unclear whether iPS cells derived from different cell types are fully comparable, or whether their differentiation process is shaped by the tissue type the cells originally came from.

To settle the matter, researchers from the University of Helsinki

compared the characteristics of iPS cells derived from skin to those derived from blood using a comprehensive range of analysis methods: in addition to gene expression, they studied DNA methylation as well as the spontaneous and guided differentiation capacity of the stem cells.

The researchers focused on determining whether human iPS cells had, as indicated by previous studies, an "epigenetic memory", meaning that a stem cell derived from a blood cell would be easier to turn into a blood cell than a stem cell derived from skin.

The results were unambiguous: several different indicators showed that the type of original cell made no difference when the stem cell was fully reprogrammed.

Says Professor Timo Otonkoski from the University of Helsinki: "It is obvious that pluripotent stem cells derived from different cell types are fully equal. These results are highly significant to biobanks, as this way one collection can feature different source cells, and previously stored living cell samples remain useful for iPS cell production."

What was surprising was how different the iPS cells derived from different individuals were. The genotype of the donor obviously shapes the differentiation behaviour of the stem cell.

"The genetically determined individual differences in stem cell differentiation were surprisingly extensive," Otonkoski points out. "This means that to make reliable observations about the functional implications of genotypes related to an illness requires that bio banks acquire a sufficiently large variety of samples from several donors."

More information: Aija Kyttälä, Roksana Moraghebi, Cristina Valensisi, Johannes Kettunen, Colin Andrus, Kalyan Kumar Pasumarthy, Mahito Nakanishi, Ken Nishimura, Manami Ohtaka, Jere Weltner, Ben

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